

U.S.S.N. 09/067,337

KOSTER et al.

**PRELIMINARY AMENDMENT**

*B6*  
*Concl'd*

~~di~~alkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, perfluoroalkoxy, alkenyloxy, alkynyoxy, arylalkoxy, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylamino, dialkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, arylcarbonylamino, aryloxycarbonylamino, azido, alkylthio, arylthio, perfluoroalkylthio, thiocyanato, isothiocyanato, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl or diarylaminosulfonyl; R<sup>20</sup> is alkylene, alkenylene, alkynylene, arylene or heteroarylene; k is 2 or 3; and j is 0 or 1.

*B6*  
49. (Amended) The LPC of claim 5 coupled to a biopolymer.

**REMARKS**

This Preliminary Amendment accompanies a request for a Continued Prosecution Application under 37 CFR 1.53(d). A check for the filing fee for a Continued Prosecution Application and a three month extension of time accompanies this response. Any fees that may be due in connection with this application may be charged to Deposit Account No. Deposit Account No. 50-1213. If a Petition for extension of time is needed, this paper is to be considered such Petition.

Claims 1-49 are presently pending in this application. Claims 1-4 are cancelled herein without prejudice or disclaimer. Applicant reserves the right to file divisional applications directed to any cancelled subject matter.

Claims 5, 8, 27, 29-32, 43-45 and 49 are amended. Claims 5, 8, 27, 31 and 45 have been rewritten as independent claims incorporating the limitations of the base claims. Claims 29, 30, 32, 43 and 44 are amended to be dependent on a pending claim. No amendments have been made to avoid any art of record. No new matter has been added.

**U.S.S.N. 09/067,337**  
**KOSTER et al.**  
**PRELIMINARY AMENDMENT**

**REQUIREMENT FOR ELECTION OF SPECIES**

Applicant elected Species A, represented by formula 1a, for search purposes in response to the previous Action. Applicant respectfully submits that the previous action was a Requirement for Election of Species, not a Restriction Requirement. Since no art was cited, generic subject matter should be allowable. Applicant has, therefore, retained claims 10-26, withdrawn from consideration, in this application. It is respectfully requested that withdrawn claims 10-26 be examined herein since the remaining claims are in condition for allowance, as described below.

**REJECTION OF CLAIMS 1-9 AND 27-49 UNDER 35 U.S.C. §112, FIRST PARAGRAPH**

Claims 1-9 and 27-49 are rejected under 35 U.S.C. §112, first paragraph, for alleged lack of enablement. It is urged that incorporation by reference to a foreign application or foreign patent or to a publication of allegedly essential material is improper. Applicant respectfully traverses this rejection.

**Relevant Law**

In order to satisfy the enablement requirement of 35 U.S.C. §112, first paragraph, the specification must teach one of skill in the art to make and use the invention. Atlas Powder Co. v. E.I. DuPont de Nemours, 750 F.2d 1569, 224 USPQ 409. That some experimentation is needed, does not preclude enablement as long such experimentation is not undue. In re Marzocci et al., 469 USPQ 367 (CCPA 1971).

The amount of experimentation that is permissible depends upon a number of factors, which include: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability of the art, and the breadth of the claims. Ex parte Forman, 230 USPQ 546 (Bd. Pat. App. & Int'l 1986); see also In re Wands, 8 USPQ2d 1400 (Fed. Cir. 1988).

**U.S.S.N. 09/067,337**  
**KOSTER et al.**  
**PRELIMINARY AMENDMENT**

Patents are written to enable those skilled in the art to practice the invention. A patent need not disclose what is well known in the art. W.L. Gore & Assoc. v. Gorlock, Inc., 721 F.2d 1540, 1556, 220 USPQ 303, 315.

To limit the claims involving the specific materials disclosed in the examples so that a competitor seeking to avoid infringing the claims can merely follow the disclosure and substitute is contrary to the purpose for which the patent system exists - to promote progress in the useful arts. In re Goffe, 542 F.2d 801, 166 USPQ 85 (CCPA 1970).

An assertion by the PTO that the enabling disclosure is not commensurate in scope with the protection sought must be supported by evidence or reasoning substantiating the doubts expressed. In re Armbruster, 512 F2d 676, 185 USPQ 152 (CCPA 1975).

The requirements of 35 USC §112, first paragraph can be fulfilled by the use of illustrative examples or by broad terminology. In re Anderson, 176 USPQ 331, 333 (CCPA 1973):

...we do not regard section 112, first paragraph, as requiring a specific example of everything within the scope of a broad claim . . . What the Patent Office is here apparently attempting is to limit all claims to the specific examples, notwithstanding the disclosure of a broader invention. This it may not do.

See also, In re Grimme, Keil and Schmitz, 124 USPQ 449, 502 (CCPA 1960) :

It is manifestly impracticable for an applicant who discloses a generic invention to give an example of every species falling within it, or even to name every such species. It is sufficient if the disclosure teaches those skilled in the art what the invention is and how to practice it.

The law does not require an applicant to describe in the specification every conceivable embodiment of the invention. SRI Int'l v. Matsushita Elec. Corp of America, 775 F.2d 1107, 1121, 227 USPQ 577, 586 (Fed. Cir. 1985).

**U.S.S.N. 09/067,337**  
**KOSTER et al.**  
**PRELIMINARY AMENDMENT**

**Analysis**

**Incorporation by Reference**

It is alleged that incorporation by reference to non-patent publications is improper because the material described in the articles includes essential subject matter related to the description of linker molecules (page 37) and methods for the synthesis protocols for biopolymers (page 46, lines 23 and 24). Applicant respectfully submits that the articles referred to in the cited passages do not include essential subject matter because the incorporated references merely provide examples of linkers and methods of biopolymer synthesis that are well known to those of skill in the art.

**Linkers**

The specification at page 36, line 1, discloses LPCs coupled to linkers. The linkers that may be coupled to the LPCs provided in the specification are any known to those of skill in the art. Such linkers are well known and are available from numerous commercial sources. As disclosed in the specification, the linkers have traditionally been used in solid phase synthesis of biopolymers, and include, for example, photocleavable, traceless, safety-catch or other linkers (see, e.g., page 36, lines 4-7). The references listed on page 36, line 7 through page 37, line 3 include publications and U.S. patents that describe linkers and are included merely to provide examples of what is well known to those of skill in the art.

**Methods for the Synthesis of Biopolymers**

The specification, at page 45, line 25, discloses that synthesis of the biopolymeric chain in the methods provided in the application may be carried out using any protocols known to those of skill in the art. Such protocols are well known. In the synthesis of oligonucleotides, protocols including the phosphate triester, H-phosphonate, or phosphoramidite protocols may be used (see, e.g., page 45, lines 27-29). These protocols are well known to those of skill in the art. The publications and U.S. patents listed at page 45, line 29

U.S.S.N. 09/067,337

KOSTER et al.

**PRELIMINARY AMENDMENT**

through page 46, line 7 are included merely to provide examples of what is well known to those of skill in the art.

Similarly, references are provided for synthetic protocols for preparation of peptides, peptide nucleic acids and oligosaccharides merely to give examples of what is well known to those of skill in the art (see, e.g., page 46, lines 10-22).

**The Cited References do not contain Essential Subject Matter**

None of these cited references contains subject matter essential to the instant claims. The references merely provide examples of what is well known to those of skill in the art. Other linkers or biopolymer synthetic protocols can be used in the compositions and methods encompassed by the instant claims. Patents are written to enable those skilled in the art to practice the invention. A patent need not disclose what is well known in the art. W.L. Gore & Assoc. v. Gorlock, Inc., 721 F.2d 1540, 1556, 220 USPQ 303, 315.

Therefore, since the references provided in the specification on page 36 line 7 through page 37, line 3, and on page 45, line 29 through page 46, line 22 are not essential material, but merely exemplify what is well known to those of skill in the art, it is not necessary to amend the disclosure to include the material incorporated by reference. Applicant respectfully requests reconsideration and removal of this rejection.

**Scope of X<sup>1</sup>**

The Office Action also alleges that there is not seen in the disclosure support commensurate in scope with the description of the variable X<sup>1</sup> to be represented by "any reactive group which can be used in biopolymer synthesis." It is urged that there is support for X<sup>1</sup> to be represented by OH, SH, NH<sub>2</sub>, COR<sup>5</sup> and COOR<sup>4</sup>, but not any reactive group. Applicant respectfully disagrees.

It is first noted that X<sup>1</sup> is not defined as "any reactive group." X<sup>1</sup> is defined in the specification and claims as "any reactive group which can be used in biopolymer synthesis" (see, e.g., claim 5 and the specification at page

U.S.S.N. 09/067,337  
KOSTER et al.  
PRELIMINARY AMENDMENT

4, lines 16 and 17).  $X^1$  is further defined in the specification and claims to include, but not be limited to, halide, preferably chloride, OH, SH, NH<sub>2</sub>, COR<sup>5</sup> and COOR<sup>4</sup>, where R<sup>4</sup> is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclalkyl, and R<sup>5</sup> is halide, heteroaryl, aryl or pseudohalide. (see, e.g., page 26, lines 19-21, page 31, lines 10-15, and claim 6).

As stated in In re Anderson, 176 USPQ 331, 333 (CCPA 1973):

...we do not regard section 112, first paragraph, as requiring a specific example of everything within the scope of a broad claim . .

. What the Patent Office is here apparently attempting is to limit all claims to the specific examples, notwithstanding the disclosure of a broader invention. This it may not do.

See also, In re Grimme, Keil and Schmitz, 124 USPQ 449, 502 (CCPA 1960) :

It is manifestly impracticable for an applicant who discloses a generic invention to give an example of every species falling within it, or even to name every such species. It is sufficient if the disclosure teaches those skilled in the art what the invention is and how to practice it.

Furthermore, the law does not require an applicant to describe in the specification every conceivable embodiment of the invention. SRI Int'l v. Matsushita Elec. Corp of America, 775 F.2d 1107, 1121, 227 USPQ 577, 586 (Fed. Cir. 1985).

Therefore, it is not necessary that the specification provide support for all of the embodiments within the scope of the instant claims. Nor is it necessary that the specification provide an example of every species falling within the scope of  $X^1$ , as defined. It is only required that the specification teach those skilled in the art what the invention is and how to practice it. In the present case,  $X^1$  is any reactive group useful in biopolymer synthesis. Such reactive groups are well known to those of skill in the art, who generally are those with advanced degrees in chemistry, molecular biology, or related fields. One of skill in the art would be able to practice the claimed invention based on the

U.S.S.N. 09/067,337

KOSTER et al.

**PRELIMINARY AMENDMENT**

disclosure of the specification. Therefore, the instant claims are enabled by the disclosure of the specification.

**REJECTION OF CLAIMS 1-9 AND 27-49 UNDER 35 U.S.C. §112, SECOND PARAGRAPH**

Claims 1-9 and 27-49 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Applicant respectfully requests reconsideration of this rejection in view of the amendments to the claims herein and the following remarks.

**Claims 1, 33 and 45**

Claims 1, 33 and 45 are rejected as allegedly being indefinite for failing to provide a chemical name or structural formula for Sp, n and X<sup>1</sup>. Applicant respectfully disagrees.

It is first noted that claim 1 has been cancelled herein without prejudice or disclaimer. Applicant further notes that the variables Sp and n do not appear in claim 45.

**Sp**

The variable Sp is defined in claim 33 by functional language, thereby uniquely identifying the groups encompassed by the claim. Sp is defined in claim 33 as "a polyvalent group that has more than two points of attachment." Thus, Sp is not a monovalent group, nor is it a divalent group. Sp is further defined in the specification as including, without limitation, "an atomic group, a cyclic group or an aromatic group (heterocycles, carbocycles, aryls, heteroaryls, such that the resulting structure is symmetrically disposed around the center of the cyclic group), that has more than two points of attachment" (see, e.g., page 3, lines 1-4). Sp also represents, in certain embodiments, (R<sup>1</sup>)<sub>p</sub>-A, E or a cyclic group (i.e., heterocycles, carbocycles, aryls, heteroaryls, such that the resulting structure is symmetrically disposed around the center of the cyclic group)(see, e.g., page 3, lines 31-33). Thus, the specification provides functional definitions of Sp and numerous examples (supra). Based on this disclosure, one

**PRELIMINARY AMENDMENT**

of ordinary skill in the art would be able to determine whether a given moiety was within the scope of Sp. Therefore, it is respectfully submitted that the variable Sp is not indefinite to a person having ordinary skill in the art.

**n**

The variable n in claim 33 relates to the number of points of attachment in Sp. Since, as described in detail above, the variable Sp is not indefinite, the variable n is likewise not indefinite.

**X<sup>1</sup>**

The variable X<sup>1</sup> is defined in claims 33 and 45 by functional language, thereby uniquely identifying the groups encompassed by the claim. X<sup>1</sup> is defined in claims 33 and 45 as a reactive group that may be used in biopolymer synthesis. Thus, X<sup>1</sup> does not encompass any reactive group, but only those groups that are useful in biopolymer synthesis. One of ordinary skill in the art would know what reactive groups would have such utility.

Furthermore, the specification provides non-limiting examples of such reactive groups, including, but not limited to, halide, preferably chloride, OH, SH, NH<sub>2</sub>, COR<sup>5</sup> and COOR<sup>4</sup>, where R<sup>4</sup> is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl, and R<sup>5</sup> is halide, heteroaryl, aryl or pseudohalide. (see, e.g., page 26, lines 19-21, page 31, lines 10-15).

The specification provides examples of the X<sup>1</sup> groups that are preferably used for synthesis of various biopolymers, thereby further defining the scope of X<sup>1</sup>. LPCs for use in oligonucleotide synthesis may contain, for example, a carboxylic acid group at the terminus of X<sup>1</sup> (see, e.g., page 32, lines 30-31). LPCs for use in peptide synthesis or peptide nucleic acid synthesis may contain, for example, a haloalkyl, hydroxyl, thio or carboxyl group at the terminus of X<sup>1</sup> (see, e.g., page 34, lines 13-14 and page 35, lines 15-16). LPCs for use in oligosaccharide synthesis may contain, for example, a hydroxyl, thio or carboxyl group at the terminus of X<sup>1</sup> (see, e.g., page 35, lines 24-25).

**U.S.S.N. 09/067,337**  
**KOSTER et al.**  
**PRELIMINARY AMENDMENT**

Therefore, the variable X<sup>1</sup>, when viewed in light of the specification and the knowledge of one of ordinary skill in the art, is not indefinite.

**Claims 5 and 38**

Claims 5 and 38 are rejected as allegedly being indefinite for defining the variable X<sup>1</sup> twice. Applicant respectfully submits that X<sup>1</sup> is only defined once in each claim. Claim 5 defines X<sup>1</sup> as "any reactive group which can be used in biopolymer synthesis." Claim 38 defines X<sup>1</sup> as "any reactive group which can be used in biopolymer synthesis." This variable is not further defined in either of these claims.

The Office Action states that X<sup>1</sup> is defined as "any reactive group, and the claim also recites a Markush grouping definition..." Applicant respectfully submits that claims 5 and 38 do not contain a Markush grouping definition for X<sup>1</sup>. These claims do recite a Markush group for the variables A, E, R<sup>1</sup>, R<sup>3</sup>, p, n, Y<sup>1</sup> and Y<sup>2</sup>. The claims further recite that the variables R<sup>1</sup>, R<sup>3</sup>, X<sup>1</sup>, Y<sup>1</sup>, Y<sup>2</sup> and Z are unsubstituted or substituted with one or more substituents each independently selected from Q, where Q is defined by a Markush group. Thus, the claims define a Markush group for the substituents that may be present on X<sup>1</sup>, but does not recite a Markush group for X<sup>1</sup> itself. Applicant respectfully requests reconsideration and withdrawal of this rejection.

**Claim 8**

Claim 8 is rejected as allegedly being indefinite for not separating the structural formulae with commas. In claim 8, as amended herein, the structural formulae are separated with commas. Applicant respectfully requests reconsideration and withdrawal of this rejection.

**Claim 33**

Claim 33 is rejected as allegedly being indefinite because the variable N<sup>m</sup> is allegedly not defined. Applicant respectfully disagrees. The claim recites "N<sup>1</sup>, N<sup>2</sup>, N<sup>3</sup>...N<sup>m</sup> are biopolymer monomers." Thus, N<sup>m</sup> is a biopolymer

**U.S.S.N. 09/067,337**  
**KOSTER et al.**  
**PRELIMINARY AMENDMENT**

monomer. Furthermore, m is defined as "3 to 100," thereby defining the length of the biopolymer chain.

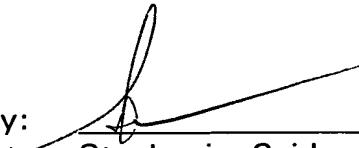
It is further alleged that claim 33 is confusing where in the last line of the claims "dimers and trimers are monomers." Applicant respectfully disagrees. The last line of instant claim 33 recites "the dimers and trimers comprise the monomers" (emphasis added). Therefore, the "dimers" and "trimers" of claim 33 are not monomers, but rather are comprised of the monomers. A dimer comprises two monomers and a trimer comprises three monomers.

Applicant respectfully submits that claim 33 is not indefinite for the reasons stated above. Reconsideration and withdrawal of this rejection is respectfully requested.

\* \* \*

In view of the above, reconsideration and allowance of the application is respectfully requested.

Respectfully submitted,  
HELLER EHRMAN WHITE & McAULIFFE

By:   
Stephanie Seidman  
Registration No. 33, 779

Attorney Docket No. 24743-2301  
Address all correspondence to:  
Stephanie Seidman, Esq.  
HELLER EHRMAN WHITE & McAULIFFE  
4250 Executive Square, 7th Floor  
La Jolla, California 92037  
Telephone: 858 450-8400  
Facsimile: 858 587-5360  
email: [sseidman@HEWM.com](mailto:sseidman@HEWM.com)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Koster et al.

Serial No.: 09/067,337

Confirmation No.: 9981

Filed: April 27, 1998

For: *SOLUTION PHASE BIOPOLYMER  
SYNTHESIS*

Art Unit: 1623

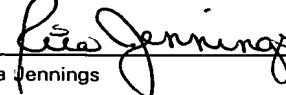
Examiner: Wilson, J.

CERTIFICATE OF MAILING BY "EXPRESS MAIL"

"Express Mail" Mailing Label Number  
EL675147920US

Date of Deposit March 12, 2001

I hereby certify that this paper and the attached papers are being deposited with the United States Postal "Express Mail Post Office to Addressee" Service under 37 C.F.R. §1.10 on the date indicated above and addressed to: Commissioner for Patents, BOX CPA, Washington, D.C. 20231

  
Rita Jennings

**ATTACHMENT TO PRELIMINARY AMENDMENT**

The following attachment is provided:

- (1) a marked up copy of claims 5, 8, 27, 29-32, 43-45 and 49 showing the amendments herein.

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: Koster et al.

Serial No.: 09/067,337

Confirmation No.: 9981

Filed: April 27, 1998

For: **SOLUTION PHASE BIOPOLYMER  
SYNTHESIS**

Art Unit: 1623

Examiner: Wilson, J.



CERTIFICATE OF MAILING BY "EXPRESS MAIL"

"Express Mail" Mailing Label Number  
EL675147920US

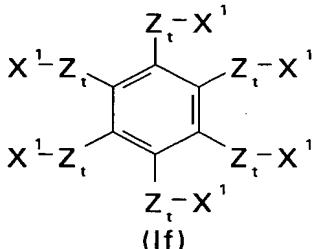
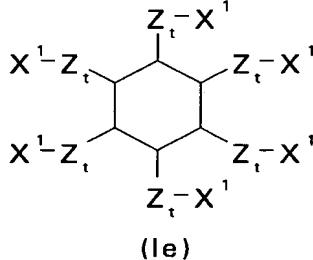
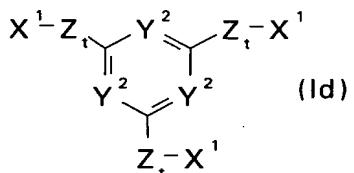
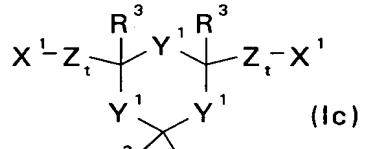
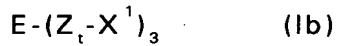
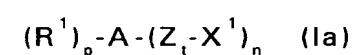
Date of Deposit March 12, 2001

I hereby certify that this paper and the attached papers are being deposited with the United States Postal "Express Mail Post Office to Addressee" Service under 37 C.F.R. §1.10 on the date indicated above and addressed to: Commissioner for Patents, BOX CPA, Washington, D.C. 20231

  
Rita Jennings

**MARKED UP CLAIMS (37 CFR §1.121)**

5. (Amended) A liquid phase carrier (LPC) [The LPC of claim 1] that has formulae (I):



wherein: A is carbon or silicon; E is nitrogen or P(O); R<sup>1</sup> and R<sup>3</sup> are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; p is 0 or 1; Z is any combination of 1-12 units selected from 1,2-, 1,3- or 1,4-phenylene and alkylene units, which units may be combined in any order, with the proviso that if the LPC is of formula (Ia) or

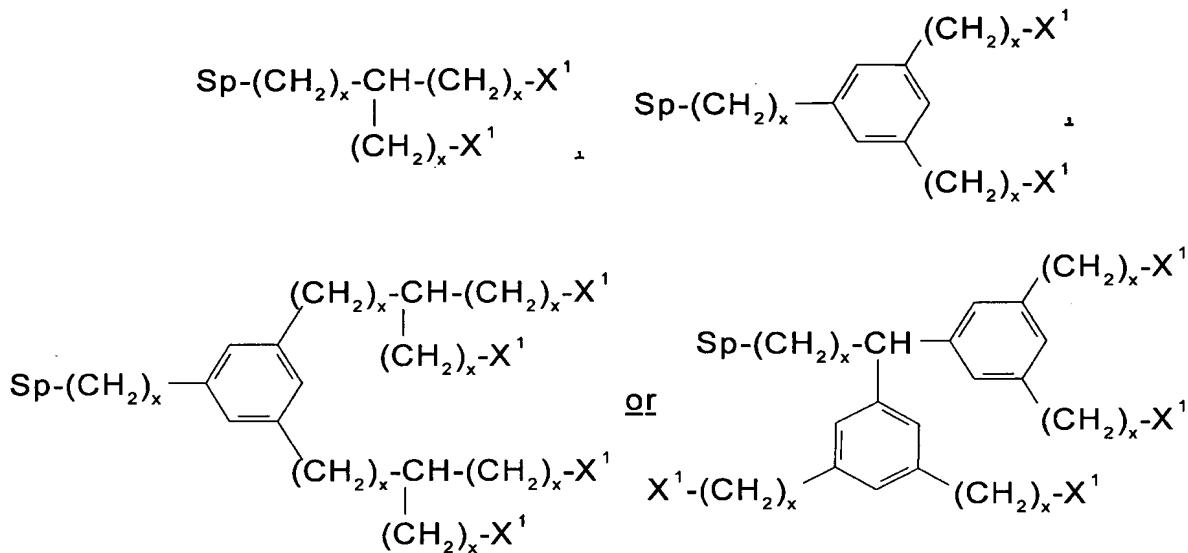
U.S.S.N. 09/067,337

KOSTER et al.

MARKED UP CLAIMS (37 CFR §1.121)

(Ib), then Z contains at least two phenylene or methylene units; t is 1; X<sup>1</sup> is any reactive group which can be used in biopolymer synthesis; n is 3 or 4; Y<sup>1</sup> is CH<sub>2</sub>, NH, S or O; Y<sup>2</sup> is selected from CH and N; R<sup>1</sup>, R<sup>3</sup>, X<sup>1</sup>, Y<sup>1</sup>, Y<sup>2</sup> and Z are unsubstituted or substituted with one or more substituents each independently selected from Q; and Q is halogen, hydroxy, nitrile, nitro, formyl, mercapto, carboxy, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, perfluoroalkoxy, alkenyloxy, alkynyoxy, arylalkoxy, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylamino, dialkylamino, arylamino, diarylamino, alkylaryl amino, alkylcarbonyl amino, alkoxy carbonyl amino, arylcarbonyl amino, aryloxycarbonyl amino, azido, alkylthio, arylthio, perfluoroalkylthio, thiocyanato, isothiocyanato, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl or diarylaminosulfonyl.

8. (Amended) A liquid phase carrier (LPC) [The LPC of claim 1], wherein the LPC has any of formulae:



[where in] wherein: Sp is a polyvalent group that has more than two points of attachment, X' is a reactive group for synthesis of biopolymers, and x is 0-6.

27. (Amended) A liquid phase carrier (LPC) [The LPC of claim 1], wherein the LPC has formula  $Sp(O-(CH_2)_2-C(O)-NH-(CH_2)_x-NH_2)_n$ ,  $Sp(S-(CH_2)_2-C(O)-NH-(CH_2)_x-NH_2)_n$ ,  $Sp(O-(CH_2)_2-C(O)-NH-(CH_2)_x-NH-C(O)-(CH_2)_x-COOH)_n$ ,  $Sp(S-(CH_2)_2-C(O)-NH-(CH_2)_x-NH-C(O)-(CH_2)_x-COOH)_n$ ,  $Sp(NH-C(O)-(CH_2)_x-COOH)_n$ ,  $Sp(C(O)-NH-(CH_2)_x-NH_2)_n$ ,  $Sp(C(O)-NH-(CH_2)_x-NH-C(O)-(CH_2)_x-COOH)_n$ ,  $Sp(O-(CH_2)_2-C(O)-O-(CH_2)_x-OH)_n$ ,  $Sp(O-(CH_2)_2-C(O)-O-(CH_2)_x-SH)_n$ ,  $Sp(S-(CH_2)_2-C(O)-O-(CH_2)_x-OH)_n$ ,  $Sp(S-(CH_2)_2-C(O)-O-(CH_2)_x-SH)_n$ ,  $Sp(S-(CH_2)_2-C(O)-S-(CH_2)_x-OH)_n$ ,  $Sp(O-(CH_2)_2-C(O)-S-(CH_2)_x-SH)_n$ ,  $Sp(NH-C(O)-(CH_2)_x-CO-O-(CH_2)_x-OH)_n$ ,  $Sp(NH-C(O)-(CH_2)_x-CO-O-(CH_2)_x-SH)_n$ ,  $Sp(NH-C(O)-(CH_2)_x-CO-S-(CH_2)_x-OH)_n$ ,  $Sp(C(O)-O-(CH_2)_x-OH)_n$ ,  $Sp(C(O)-S-(CH_2)_x-OH)_n$ ,  $Sp(C(O)-O-(CH_2)_x-SH)_n$  or  $Sp(C(O)-S-(CH_2)_x-SH)_n$  where x is 0-6, Sp is a polyvalent group that has more than two points of attachment, and n is the number of points of attachment.

U.S.S.N. 09/067,337

KOSTER et al.

MARKED UP CLAIMS (37 CFR §1.121)

29. (Amended) The LPC of claim [1] 5 that is coupled to a photocleavable linker.

30. (Amended) The LPC of claim [1] 27 selected from the group consisting of  $Sp(O-(CH_2)_2-C(O)-NH-(CH_2)_x-NH-C(O)-(CH_2)_x-COOH)_n$ ,  $Sp(S-(CH_2)_2-C(O)-NH-(CH_2)_x-NH-C(O)-(CH_2)_x-COOH)_n$ ,  $Sp(NH-C(O)-(CH_2)_x-COOH)_n$  and  $Sp(C(O)-NH-(CH_2)_x-NH-C(O)-(CH_2)_x-COOH)_n$ , where  $x$  is 0-6.

31. (Amended) A liquid phase carrier (LPC) [The LPC of claim 1], selected from the group consisting of tetrakis(8-amino-6-aza-2-oxa-5-oxooctyl)methane, tetrakis(11-carboxy-6,9-diaza-5,10-dioxo-2-oxaundecyl)methane, tris(3-aza-6-carboxy-4-oxohexyl)amine, 1,3,5-benzenetricarboxylic acid tris-N-(2-aminoethyl)amide, 1,3,5-benzenetricarboxylic acid tris-N-(3-aza-6-carboxy-4-oxohexyl)amide, tetrakis{6,9-diaza-13-[5'-O-(4,4'-dimethoxytriphenylmethyl)-2'-deoxythymidine-3'-O-yl]-2-oxa-5,10,13-trioxotridecyl}methane ((DMT-dT)<sub>4</sub>-PE-LPC), 1,3,5-tris{2,5-diaza-9-[5'-O-(4,4'-dimethoxytriphenyl-methyl)-2'-deoxythymidine-3'-O-yl]-1,6,9-trioxononyl}-benzene ((DMT-dT)<sub>3</sub>-Aryl-LPC), tetrakis[13-(2'-deoxythymidin-3'-O-yl)-6,9-diaza-2-oxa-5,10,13-trioxotridecyl]-methane (dT<sub>4</sub>-PE-LPC), 1,3,5-tris[9-(2'-deoxythymidin-3'-O-yl)-2,5-diaza-1,6,9-trioxononyl]-benzene (dT<sub>3</sub>-Aryl-LPC), tris-{3-aza-4,7-dioxo-7-[5'-O-(4,4'-dimethoxytriphenylmethyl)-2'-deoxythymidine-3'-O-yl]-heptyl}-amine ((DMT-dT)<sub>3</sub>-Amine-LPC) and tris[3-aza-7-(2'-deoxythymidine-3'-O-yl)-4,7-dioxohexyl]-amine (dT<sub>3</sub>-Amine-LPC).

32. (Amended) The LPC of claim [1] 31 selected from the group consisting of tetrakis(11-carboxy-6,9-diaza-5,10-dioxo-2-oxaundecyl)methane, tris(3-aza-6-carboxy-4-oxohexyl)amine, 1,3,5-benzenetricarboxylic acid tris-N-(3-aza-6-carboxy-4-oxohexyl)amide, tetrakis{6,9-diaza-13-[5'-O-(4,4'-dimethoxytriphenylmethyl)-2'-deoxythymidine-3'-O-yl]-2-oxa-5,10,13-trioxotridecyl}methane ((DMT-dT)<sub>4</sub>-PE-LPC), 1,3,5-tris{2,5-diaza-9-[5'-O-(4,4'-dimethoxytriphenyl-methyl)-2'-deoxythymidine-3'-O-yl]-1,6,9-trioxononyl}-benzene ((DMT-dT)<sub>3</sub>-Aryl-LPC), tetrakis[13-(2'-deoxythymidin-3'-O-yl)-6,9-diaza-

U.S.S.N. 09/067,337

KOSTER et al.

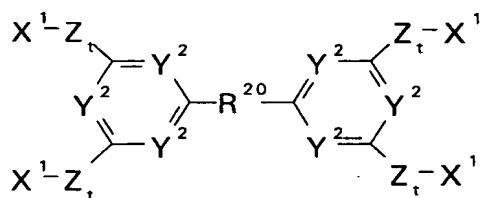
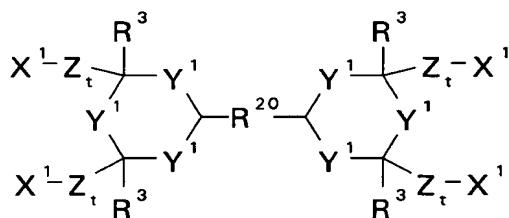
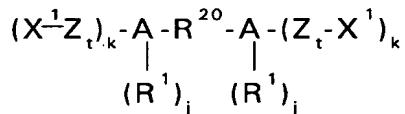
MARKED UP CLAIMS (37 CFR §1.121)

2-oxa-5,10,13-trioxotridecyl]-methane (dT<sub>4</sub>-PE-LPC), 1,3,5-tris[9-(2'-deoxythymidin-3'-O-yl)-2,5-diaza-1,6,9-trioxononyl]-benzene (dT<sub>3</sub>-Aryl-LPC), tris-{3-aza-4,7-dioxo-7-[5'-O-(4,4'-dimethoxytriphenylmethyl)-2'-deoxythymidine-3'-O-yl]-heptyl}-amine ((DMT-dT)<sub>3</sub>-Amine-LPC) and tris[3-aza-7-(2'-deoxythymidine-3'-O-yl)-4,7-dioxoheptyl]-amine (dT<sub>3</sub>-Amine-LPC).

43. (Amended) The LPC of claim [1] 32 selected from the group consisting of tetrakis[13-(2'-deoxythymidin-3'-O-yl)-6,9-diaza-2-oxa-5,10,13-trioxotridecyl]-methane (dT<sub>4</sub>-PE-LPC), 1,3,5-tris[9-(2'-deoxythymidin-3'-O-yl)-2,5-diaza-1,6,9-trioxononyl]-benzene (dT<sub>3</sub>-Aryl-LPC), and tris[3-aza-7-(2'-deoxythymidine-3'-O-yl)-4,7-dioxoheptyl]-amine (dT<sub>3</sub>-Amine-LPC).

44. (Amended) The LPC of claim [1] 43 that is 1,3,5-tris[9-(2'-deoxythymidin-3'-O-yl)-2,5-diaza-1,6,9-trioxononyl]-benzene (dT<sub>3</sub>-Aryl-LPC).

45. (Amended) A liquid phase carrier (LPC) [The LPC of claim 1] that has formulae:



U.S.S.N. 09/067,337

KOSTER et al.

MARKED UP CLAIMS (37 CFR §1.121)

wherein: A is carbon or silicon; E is nitrogen or P(O); R<sup>1</sup> and R<sup>3</sup> are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; Z is any combination of 1-12 units selected from 1,2-, 1,3- or 1,4-phenylene and alkylene, which units may be combined in any order, with the proviso that if the LPC is of formula (Ia) or (Ib), then Z contains at least two phenylene or methylene units; t is 0 or 1; X<sup>1</sup> is any reactive group which can be used in biopolymer synthesis; Y<sup>1</sup> is CH<sub>2</sub>, NH, S or O; Y<sup>2</sup> is selected from CH and N; R<sup>1</sup>, R<sup>3</sup>, X<sup>1</sup>, Y<sup>1</sup>, Y<sup>2</sup> and Z are unsubstituted or substituted with one or more substituents each independently selected from Q; and Q is halogen, hydroxy, nitrile, nitro, formyl, mercapto, carboxy, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, aryl, heteroaryl, arylalkyl, heteroarylalkyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonyl-alkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, perfluoroalkoxy, alkenyloxy, alkynyoxy, arylalkoxy, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylamino, dialkylamino, arylamino, diarylamino, alkylarylarnino, alkylcarbonylarnino, alkoxycarbonylarnino, arylcarbonylarnino, aryloxycarbonylarnino, azido, alkylthio, arylthio, perfluoroalkylthio, thiocyanato, isothiocyanato, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl or diarylaminosulfonyl; R<sup>20</sup> is alkylene, alkenylene, alkynylene, arylene or heteroarylene; k is 2 or 3; and j is 0 or 1.

49. (Amended) The LPC of claim [1] 5 coupled to a biopolymer.